Cancer Research Center Hotline

SELECT (Opportunity for Prostate Cancer Prevention)

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Cancer primary prevention clinical trials are different from disease-specific treatment trials. Prevention trials typically 1) include participants who are otherwise healthy, devoid of symptoms and thus require that toxicities or side effects from any intervention be minimal, 2) require large numbers of subjects to detect a difference between the intervention and control groups, and 3) require long study and follow-up periods to detect differences in outcomes related to all-cause survival, cancer-specific survival and quality of life. SELECT, the Selenium and Vitamin E Cancer Prevention Trial presented here, offers the opportunity to men in Hawaii to participate in a clinical trial and contribute to our scientific understanding and control of prostate cancer.

Carcinoma of the prostate is the most common tumor in the United States with 189,000 new cases and 30,200 deaths expected in 2002. In Hawaii, estimates for prostate cancer in 2002 are 700 new cases and 100 prostate cancer-related deaths.[1] Histologic evidence of the disease may occur in as many of 34% of men in their fifth decade, and up to 70% of men 80 years of age and older. While one in five U.S. men will be diagnosed with prostate cancer during his lifetime, only 3% of men are expected to die of the disease. The menu of treatment options for localized prostate cancer includes radical prostatectomy, external-beam radiation therapy, brachytherapy, hormonal treatments or surveillance. Issues that confound the choice of treatment include side effects of treatment, the inability to predict the natural history of a given cancer, and patient comorbid conditions that may ultimately affect the patient's likelihood of succumbing to prostate cancer morbidity and mortality. The question of whether screening digital rectal examination and PSA improve mortality and morbidity awaits the results of ongoing clinical trials such as the Prostate, Lung, Colon, and Ovarian (PLCO) trial sponsored by the National Cancer Institute. However, prostate screening appears to have resulted in a substantial stage migration in diagnosed prostate cancers to earlier, potentially curable stages; metastatic prostate cancer at initial diagnosis may become a historical footnote.

Factors that increase the risk for prostate cancer include increasing age, prostate cancer in first degree male relatives, the male hormonal testosterone milieu, race and dietary fat. Some studies associate increased dietary intake of fruits and vegetables with a reduced risk of prostate cancer.

Although it may be increasingly evident that dietary choices play a role in the development of prostate and other cancers, changing patterns of dietary behavior and life-long intervention makes this strategy difficult in practice. Since the 1980's, chemoprevention, the use of natural or synthetic substances to reduce the risk of developing cancer, has become an important focus of National Cancer Institute-sponsored clinical trials. Since the development of prostate cancer appears to be age-dependent, any intervention that reduces the incidence of clinically significant disease by five, 10 or 15 years would significantly reduce prostate cancer morbidity and mortality. For the chemoprevention of prostate cancer, a number of options have been considered: retinoids, DFMO, inhibitors of cholesterol biosynthesis, alpha-tocopherol, anti-androgens and 5-alpha reductase inhibitors.[2] Recognition of the importance of the androgenic milieu on the prostate in the development of prostate cancer resulted in the Prostate Cancer Prevention Trial (PCPT) using finasteride (Proscar). This trial began accrual in October 1993 and ended in May 1997 with enrollment of over 18,000 participants nationwide. The study tests the ability of finasteride, a 5-alpha reductase inhibitor, on reducing prostate gland dihydrotestosterone and, hence, a possible reduction in the incidence of prostate cancer. Final analysis is expected in 2004.

Primary prevention of prostate cancer through dietary supplementation now appears to be a promising strategy to reduce the morbidity and mortality of this disease. Secondary analyses of data from two prospective, randomized cancer prevention trials with selenium and vitamin E suggested these two agents for a second large-scale clinical trial. In a clinical trial conducted by Clark et al., prostate cancer incidence was reduced by two-thirds among men receiving daily selenium supplementation.[3] In the Alpha-Tocopherol, Beta-Carotene (ATBC) Cancer Prevention Study carried out in Finland, there was a one-third reduction in prostate cancer incidence and a 40% reduction in prostate cancer mortality in men randomized to receive vitamin E.[4] A confirmatory trial, SELECT, the Selenium and Vitamin E Cancer Prevention Trial, with prostate cancer incidence as one of the primary endpoints will substantiate these findings.

The primary objective of SELECT is to assess the effect of selenium and vitamin E, either alone or in combination, on the incidence of prostate cancer diagnosed during routine clinical practice. Secondary objectives include assessing the impact of selenium and vitamin E on the incidence of lung cancer, colon cancer and all other cancers; on cancer-specific survival and overall survival. Quality of life, evaluation of molecular and genetic markers of cancer risk, other biomarkers, and measures of nutrient intake will also be assessed. An ancillary study called PREADVISE for Prevention of Alzheimer's Disease by Vitamin E and Selenium Trial, will recruit from the SELECT participant pool, screening for changes in short-term memory or other forms of dementia.

Enrollment to SELECT, a National Cancer Institute-sponsored trial, began in July 2002. More than 32,000 men at over 400 sites in the United States, Puerto Rico, and Canada will be recruited. Enrollment is estimated to take five years, with the entire duration of the trial being 12 years. The University of Hawaii Minority-Based Clinical Oncology Program, administered by the Cancer Research Center of Hawaii, is one of the sites selected to conduct this study.

Eligible males must be age 55 or older (age 50 and older for African-American men), have had a non-suspicious DRE and a total PSA less than or equal to 4.0 ng/ml within 364 days of randomiza-

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intended to provide paraprofessionals working in elder care with background information about aging. The workshop for home health aides, care aides and adult day care assistants on the Big Island includes the following five training modules: the aging process, health and wellness, illness and disability, basic caregiving skills, and death, dying and bereavement.

In 2002, the COA embarked on a strategic planning process to determine how to better serve the Center's constituents. The primary commitment is to serve the University of Hawaii system, including students, staff, and faculty. As academics, the staff creates and disseminates new knowledge. As a state-supported educational unit, however, it is responsible to state and local agencies to improve the quality of life for adults and elders, as well as to recognize and help meet the needs of the aging public.

For more information on the Center on Aging, call 956-5001 or visit the web site at www.hawaii.edu/aging.

References

1. *Growing Old in a New Age.* (1993). Video Series 1 – 13. University of Hawaii at Manoa. Honolulu, Hawaii.
2. Montgomery, R.J. & Kosloski, K. D. (2000). *Family care giving: Change, continuity, and diversity.* In Lawton, P. & Rubernstein, L. (Eds.). (2000). Interventions in dementia care. New York: Spring Publishing.

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tion. (Additional eligibility criteria may be obtained by contacting the study site.) Participants will receive either 200 mcg of selenium, 400 mg of vitamin E, both, or placebos for up to 12 years. Blood samples and toenail clippings will be requested from all participants. Participants will also be asked to take part in the PREADVISE. However, declining to provide samples or to take part in the PREADVISE will not affect their participation in SELECT.

For more information in Hawaii, contact the Clinical Trials Unit, (808)586-2979. For information on study sites outside of Hawaii, call the Cancer Information Service of Hawaii at 1-800-4-CANCER. In Canada, call the Canadian Cancer Society's Cancer Information Service at 1-888-939-3333.

References

1. American Cancer Society: Cancer Facts and Figures-2002. Atlanta, GA: American Cancer Society, 2002.
2. Thompson IM, Coltman CA, Brawley OW, et al. Chemoprevention of prostate cancer. Seminars in Urology XIII, No. 2: 122-129, 1995.
3. Clark LC, Combs GF Jr, Turnbull BW, et al. Effects of selenium supplementation for cancer prevention in patients with carcinoma of the skin. A randomized controlled trial. Nutritional Prevention of Cancer Study Group. JAMA 276:1957-1963, 1996.
4. Heinonen OP, Albanes D, Huttunen JK, et al. Prostate cancer and supplementation with alpha-tocopherol and betacarotene: incidence and mortality in a controlled trial. J Natl Cancer Inst 90:440-6, 1998.

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